

## REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### Claim Amendments

Claims 1-3, 24-26 have been amended to clarify that the reagents are directly labeled with differential isotopes.

Claims 1-3, 5, 24-26, and 28-29 have been amended to clarify language of “isotopically labeled” by replacing with the phrase “differential isotope labeled reagents.”

Claims 1-4, 6, 8-10, 12-14, 21 were amended to remove the reference to “derivatized molecules in a preparation,” “preparation,” and replace with the term “derivatives” for clarity.

Claims 1-3, 5, 15, 24-26, and 28-29 were amended to correct the spelling of “labeled.”

Claims 1 and 24 have been amended to remove the term “a set” for clarity.

Claims 4, 5, 8, 10, 12 and 27 were amended to include the recitation of “the step of” for clarity.

Claim 18 was amended to clarify that that the claim refers to any of the samples in claim 1, 2 or 3.

Claims 2-3, 25-26 and 29 have been amended to replace the term “the reductive alkylation” with the term “a reductive alkylation” to provide proper antecedent basis.

Claims 2-3, 25-26, and 29 have been amended to recite the “amine” in the singular form for clarity.

Claims 6, 7, 22, and 23 were amended to recite the U.S. spelling of ionization.

Applicants hereby reserve the right to file a continuation or divisional application on the subject claimed prior to this amendment. Applicants submit that no new matter has been added by these amendments and hereby request their entry. Claim 28 is withdrawn and Claims 1-27 and 29 are now pending in the application.

**Election/Restriction**

Applicants note that restriction under 35 U.S.C. §121 was required by the Examiner. The Examiner required restriction based upon the following inventions:

Group I. Claims 1-27 and 29, drawn to methods and preparations; and

Group II. Claim 28, drawn to a kit.

Applicants hereby confirm their election of Group I, Claims 1-27 and 29 by Mr. Steve Todd on December 6, 2004, without traverse.

**Priority**

Applicants hereby confirm their claim for priority to Canadian patent application 2,393,726 under 35 U.S.C. §119(a)-(d) and (f).<sup>1</sup>

**Claim Rejections under 35 U.S.C. § 101**

Claim 27 is rejected under 35 U.S.C. §101 because the claim allegedly recites a use, without setting forth any steps involved in the process, results in an improper definition of a process.

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<sup>1</sup> To the extent necessary to assess the relevance of any potential intervening art and at the request of the Examiner, Applicants will provide a more thorough delineation of the effective date of the currently claimed invention.

In order to overcome this rejection, Applicants have amended claim 27 to recite the method steps of any of claims 1, 2, or 3. Applicants respectfully request that this rejection be withdrawn.

**Claim Rejections under 35 U.S.C. §112**

Claims 1-27 and 29 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of the rejections under 35 U.S.C. §112 will be individually addressed below.

- (i) Applicants have corrected the spelling of "labelled" in claims 1-3, 5, 15, 24-26 and 29.
- (ii) Applicants have replaced the term "differentially labelled" with the term "differential isotope labeled" in claims 1, 24 and 26. Claims 2, 3, 5, 25, and 28-29 have also been amended.
- (iii) Applicants have deleted the term "a set" from claims 1 and 24.
- (iv) Applicants have replaced the term "the derivatized molecules in a preparation" with the term "the derivatives" in claims 1 and 3. Claims 6, 8, 10, 12, 13, 14 and 21 have been amended accordingly.
- (v) Applicants have deleted the term "in a preparation" from claim 2 and replaced the term "the preparation" with "the derivatives" in claims 1, 2 and 3. Claims 4, 6, 8, 9, 10, 12, 13, 14, 21 and 29 have been amended accordingly.
- (vi) The Examiner states that in claim 1 the term "resulting in at least three differentially and isotopically labeled derivatives" is indefinite because it is stoichiometrically unclear how a reaction involving "two isotopically labeled reagents" results in three isotopically labeled derivatives.

Applicants have removed the phrase "resulting in at least three differentially and isotopically labeled derivatives" from claim 1.

(vii) Applicant has replaced the term "the reductive alkylation" with the term "a reductive alkylation" and the term "the amines" with the term "the amine" in claims 2-3, 25-26 and 29.

(viii) Applicant has amended claim 2 by removing the comma after the word "molecules," therefore making it clear that the molecules are reacted with isotopically labeled reagents.

(ix) Applicant has amended claims 4-5 and 8 by adding the term "the step of."

(x) Applicant has amended claim 11 by inserting the term "the step of."

(xi) Applicant has replaced the term "preparation" with the term "derivatives" and added a comma after the term "derivatives" in claim 14.

(xii) Applicant has amended claim 18 by inserting the term "in any of claims 1, 2 or 3." Accordingly, it is now clear that the claim refers to any sample of claims 1, 2 or 3.

(xiii) Applicant has replaced the word "amines" with the word "amine" in claim 20. In addition, Applicant has replaced the word "residues" with the word "residue."

(xiv) Applicant has amended claims 24-26 by replacing the word "of" with the word "comprising."

(xv) Applicant has amended claim 27 by inserting the term "the steps recited in." The claim now sets forth steps involved in the method/process.

In light of the amendments and the arguments presented, Applicants submit that the rejections under 35 U.S.C. §112 has been obviated and therefore request that the rejections be withdrawn.

**Claim Rejections under 35 U.S.C. § 102**

The Examiner has rejected claims 2-6, 8-15, 17-23, 25-27 and 29 as allegedly anticipated by Aebersold et al. (US 6,670,194) (hereinafter "Aebersold et al.").

Please note that the Applicants have applied this rejection to claims as currently amended (i.e. amending claims 1, 2, 3, 25-27 and 29 by inserting the term, "wherein the reagents are directly labeled").

To anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1379 (Fed. Cir. 1986).

Applicants submit that Aebersold et al. does not contain every element of the currently claimed invention, namely the directly, differential isotope labeled reagents which, when reacted with sample, result in differential isotope labeled derivatives of the sample.

Specifically, Aebersold et al. discloses a method to analyze proteins using a multi-component protein reactive reagent of the formula A-L-PRG, where A is an affinity label that selectively binds to a capture reagent, L is a linker group which is differentially labeled with one or more stable isotopes and PRG is a "protein reactive group" that selectively reacts with a protein functional group or is a substrate for an enzyme. Accordingly, in the method of Aebersold et al. the linker is labeled, not the protein reactive group (PRG). In contrast, the method of the present invention is a simple, one-step reaction which does not employ an affinity label and a linker group. In the present invention the reagents are labeled *directly*.

For example, Aebersold describes the use of an aldehyde in the context of a protein reactive group (PRG) (col. 10, lines 50-52) which would then be coupled to an isotope labeled linker (L) (col. 9, lines 60-65) and an affinity group. However, in the present invention, the isotope label (L) as well as the covalent attachment to the protein (A) is combined in one molecule (i.e., the aldehyde), thereby there is only a one component system employed in the instant invention. This greatly simplifies the chemistry involved while, at the same time,

achieving the goal of attaching different isotopic labels to different protein samples. In addition, the present invention can produce a large number of isotopically unique reagents by combinations of reagents. For example, the use of formaldehyde, deuterated formaldehyde, sodium cyanoborohydride and sodium cyanoborodeuteride, would produce eight unique reagents.

Further, the present invention does not employ a separate affinity group (A). The use of a separate affinity tag and a linker is a central component of the technology developed by Aebersold et al. They elaborate on the beneficial effects of selective enrichment (col. 14, lines 47-50).

Applicants submit that the multi-component system disclosed in Aebersold et al. does not anticipate the presently claimed invention.

In light of the arguments presented above, Aebersold et al. does not anticipate the claimed invention. As such, Applicants respectfully request its withdrawal.

#### **Rejections under 35 U.S.C. 103(a)**

Claims 1, 4-15, 17-27, and 29 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Aebersold et al. (US 6,670,194) in view of Figeys et al. (US 2002/0076817) (hereinafter “Figeys et al.”).

Claim 16 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Aebersold et al. (US 6,670,194) and Figeys et al. (US 2002/0076817) as applied to claims 1 and 15 and further in view of Vandekerckhove & Gevaert (US 6,670,194) (hereinafter “Vanderkerckhove”)

First, to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, a prior art reference (or references) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Next, the obviousness rejections will be addressed separately.

**A. Aebersold et al. in view of Figeys et al.**

Applicants submit that the Office has not met the burden required to establish a *prima facie* case of obviousness because the references cited do not teach or suggest all of the claim limitations.

As described above, Aebersold et al. does not teach the method as currently claimed. Further, the teachings of Aebersold et al. cannot have suggested the currently claimed invention due to the complexity of the multi-component system employed in Aebersold et al. In fact, the teachings of Aebersold et al. teaches away from the currently claimed invention of a simple, one-step reaction.

The citation of Figeys et al. does not cure this defect. First, Figeys et al. does not supply the necessary teachings to arrive at the currently claimed invention of a simple, one-step reaction.

Second, Figeys et al. describes a technique where two reagents can be used in various *proportions* to develop a set of three reagents suitable for the analysis of three samples. However, these three reagents are not chemically unique, i.e. they are not differential isotope labeled, as are the reagents in the present invention. For example, Figeys et al. describe the use of different *proportions* of two isotopically distinct components to label three samples, whereas the methods of the present invention teach the use of two chemically distinct compounds (for example, formaldehyde and sodium cyanoborohydride), which exist as six isotopically unique forms to label up to eight samples.

Accordingly, claim 1 is not obvious in view of Aebersold et al. and Figeys et al. because the limitation of "reacting the molecules of each sample with at least *two differential isotope labeled reagents*" has not been met by the combination of Aebersold et al. and Figeys et al.

**B. Aebersold et al. and Figeys et al. further in view of Vanderkerckhove**

The Examiner has rejected claim 16 on the basis of obviousness with regard to Aebersold et al. (US 6,670,194) in view of Figeys (US 2002/0076817) and Vanderkerckhove and Gevaert (US 2004/0005633).

For the same reasons as described above, the combination of Aebersold et al. and Figeys et al. does not teach the method of claim 1. Vanderkerckhove teaches another multi-step procedure that requires the peptides be separated into fractions prior to any chemical alteration. (col. 1, paragraph [003]). Accordingly, the combination of Aebersold et al., Figeys et al. and Vanderkerckhove does not teach the method of dependent claim 16.

In light of the arguments presented above, Applicants respectfully request that both rejections under 35 U.S.C. §103 be withdrawn.

**Conclusion**

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit

Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

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By 

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